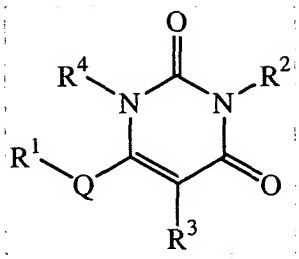
CLAIMS

What is claimed is:

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is independently selected from:

C_5 or C_6 cycloalkyl-$(C_1$-C_8 alkylenyl$)_m$;

Substituted C_5 or C_6 cycloalkyl-$(C_1$-C_8 alkylenyl$)_m$;

C_8-C_{10} bicycloalkyl-$(C_1$-C_8 alkylenyl$)_m$;

Substituted C_8-C_{10} bicycloalkyl-$(C_1$-C_8 alkylenyl$)_m$;

5- or 6-membered heterocycloalkyl-$(C_1$-C_8 alkylenyl$)_m$;

Substituted 5- or 6-membered heterocycloalkyl-$(C_1$-C_8 alkylenyl$)_m$;

8- to 10-membered heterobicycloalkyl-$(C_1$-C_8 alkylenyl$)_m$;

Substituted 8- to 10-membered heterobicycloalkyl-$(C_1$-C_8 alkylenyl$)_m$;

Phenyl-$(C_1$-C_8 alkylenyl$)_m$;

Substituted phenyl-$(C_1$-C_8 alkylenyl$)_m$;

Naphthyl-$(C_1$-C_8 alkylenyl$)_m$;

Substituted naphthyl-$(C_1$-C_8 alkylenyl$)_m$;

5- or 6-membered heteroaryl-$(C_1$-C_8 alkylenyl$)_m$;

Substituted 5- or 6-membered heteroaryl-$(C_1$-C_8 alkylenyl$)_m$;

8- to 10-membered heterobiaryl-$(C_1$-C_8 alkylenyl$)_m$;

Substituted 8- to 10-membered heterobiaryl-$(C_1$-C_8 alkylenyl$)_m$;

5- or 6-membered heterocycloalkyl-phenylenyl-$(C_1$-C_8 alkylenyl$)_m$;

Substituted 5- or 6-membered heterocycloalkyl- phenylenyl-$(C_1$-C_8 alkylenyl$)_m$;

Biphenyl-(C_1-C_8 alkylenyl)$_m$;

Substituted biphenyl-(C_1-C_8 alkylenyl)$_m$;

5- or 6-membered heteroaryl-phenylenyl-(C_1-C_8 alkylenyl)$_m$;

Substituted 5- or 6-membered heteroaryl-phenylenyl-(C_1-C_8 alkylenyl)$_m$;

5- or 6-membered heteroaryl-(5- or 6-membered heteroarylenyl)-(C_1-C_8 alkylenyl)$_m$;

Substituted 5- or 6-membered heteroaryl-(5- or 6-membered heteroarylenyl)-(C_1-C_8 alkylenyl)$_m$;

Phenyl-L-(5- or 6-membered heteroarylenyl)-(C_1-C_8 alkylenyl)$_m$;

Substituted phenyl-L-(5- or 6-membered heteroarylenyl)-(C_1-C_8 alkylenyl)$_m$;

8- to 10-membered heterobiaryl-phenylenyl-(C_1-C_8 alkylenyl)$_m$;

Substituted 8- to 10-membered heterobiaryl-phenylenyl-(C_1-C_8 alkylenyl)$_m$;

Phenyl-(5- or 6-membered heteroarylenyl)-(C_1-C_8 alkylenyl)$_m$;

Substituted phenyl-(5- or 6-membered heteroarylenyl)-(C_1-C_8 alkylenyl)$_m$;

Naphthyl-(5- or 6-membered heteroarylenyl)-(C_1-C_8 alkylenyl)$_m$;

Substituted naphthyl-(5- or 6-membered heteroarylenyl)-(C_1-C_8 alkylenyl)$_m$;

Phenyl-(8- to 10-membered heterobiarylenyl)-(C_1-C_8 alkylenyl)$_m$; and

Substituted phenyl-(8- to 10-membered heterobiarylenyl)-(C_1-C_8 alkylenyl)$_m$;

R^2 is independently selected from:

H;

C_1-C_6 alkyl;

Phenyl-(C_1-C_8 alkylenyl)$_m$;

Substituted phenyl-(C_1-C_8 alkylenyl)$_m$;

Naphthyl-(C_1-C_8 alkylenyl)$_m$;

Substituted naphthyl-(C_1-C_8 alkylenyl)$_m$;

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl)$_m$;

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl)$_m$;

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl)$_m$;

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl)$_m$;

Phenyl-O-(C_1-C_8 alkylenyl);

Substituted phenyl-O-(C_1-C_8 alkylenyl);

Phenyl-S-(C_1-C_8 alkylenyl);

Substituted phenyl-S-(C_1-C_8 alkylenyl);

Phenyl-S(O)-(C_1-C_8 alkylenyl);

Substituted phenyl-S(O)-(C_1-C_8 alkylenyl);

Phenyl-$S(O)_2$-(C_1-C_8 alkylenyl); and

Substituted phenyl-$S(O)_2$-(C_1-C_8 alkylenyl);

Each substituted R^1 and R^2 group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C_1-C_6 alkyl;

CN;

CF_3;

HO;

(C_1-C_6 alkyl)-O;

(C_1-C_6 alkyl)-S;

(C_1-C_6 alkyl)-S(O);

(C_1-C_6 alkyl)-$S(O)_2$;

O_2N;

H_2N;

(C_1-C_6 alkyl)-N(H);

(C_1-C_6 alkyl)$_2$-N;

(C_1-C_6 alkyl)-C(O)O-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)O-(1- to 8-membered heteroalkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)N(H)-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)-C(O)N(H)-(1- to 8-membered heteroalkylenyl)$_m$;

$H_2NS(O)_2$-(C_1-C_8 alkylenyl);

(C_1-C_6 alkyl)-N(H)$S(O)_2$-(C_1-C_8 alkylenyl)$_m$;

(C_1-C_6 alkyl)$_2$-$NS(O)_2$-(C_1-C_8 alkylenyl)$_m$;

3- to 6-membered heterocycloalkyl-(G)$_m$;

Substituted 3- to 6-membered heterocycloalkyl-(G)$_m$;

5- or 6-membered heteroaryl-(G)$_m$;

Substituted 5- or 6-membered heteroaryl-(G)$_m$;

$(C_1\text{-}C_6$ alkyl)-$S(O)_2$-N(H)-C(O)-$(C_1\text{-}C_8$ alkylenyl)$_m$; and

$(C_1\text{-}C_6$ alkyl)-C(O)-N(H)-$S(O)_2$-$(C_1\text{-}C_8$ alkylenyl)$_m$;

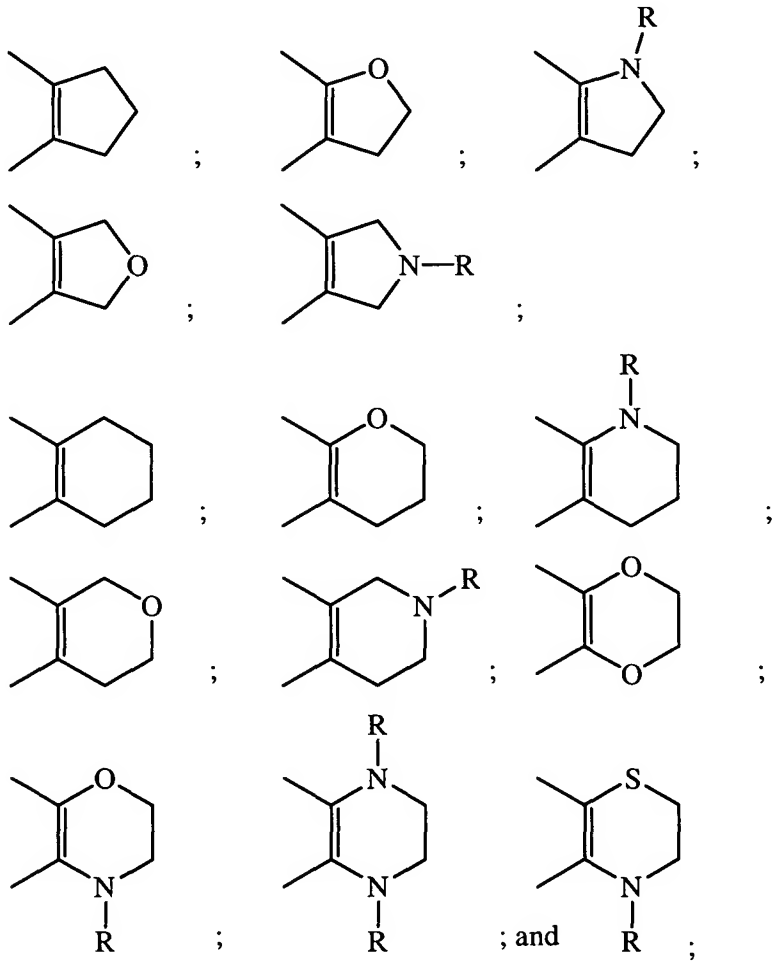
wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

HO_2C;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:



; and ;

R is H or C_1-C_6 alkyl;

G is CH_2; O, S, S(O); or $S(O)_2$;

Each m is independently selected from an integer of 0 or 1;

R^3 is independently selected from the groups:

H;

CH_3;

CH_3O;

$CH{=}CH_2$;

HO;

CF_3;

CN;

HC(O);

$CH_3C(O)$;

HC(NOH);

H_2N;

(CH_3)-N(H);

$(CH_3)_2$-N;

$H_2NC(O)$;

(CH_3)-N(H)C(O);

$(CH_3)_2$-NC(O);

Halo; and

CO_2H;

Q is independently selected from O, S, S(O), $S(O)_2$, and $N(R^5)$;

L is independently selected from CH_2, C(O), O, S, S(O), $S(O)_2$, and $N(R^6)$;

R^4, R^5, and R^6 are independently H or C_1-C_6 alkyl;

wherein each C_8-C_{10} bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 $N(C_1$-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 N(C_1-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C_1-C_6 alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any (C_1-C_6 alkyl)$_2$-N group, the C_1-C_6 alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

wherein each group and each substituent recited above is independently selected.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is O.

3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is S, S(O), or $S(O)_2$.

4. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is N(R^5), and R^5 is hydrogen or C_1-C_6 alkyl.

5. The compound according to any one of Claims 2 to 4, or a pharmaceutically acceptable salt thereof, wherein R^1 is independently selected from:

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl); and

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl); and

R^2 is independently selected from:

Phenyl-(C_1-C_8 alkylenyl)$_m$;

Substituted phenyl-(C_1-C_8 alkylenyl)$_m$;

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl)$_m$;

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl)$_m$;

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl)$_m$; and

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl)$_m$;

wherein m is an integer of 0 or 1; and

wherein each group and each substituent is independently selected.

6. The compound according to Claim 1, wherein R^2 is benzyl or substituted benzyl.

7. The compound according to Claim 1, selected from:

3-Benzyl-6-{2-[3-(2,4-dichloro-phenyl)-isoxazol-5-yl]-2-oxo-ethylsulfanyl}-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[5-(4-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[3-(4-methoxy-phenyl)-isoxazol-5-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[3-(2,6-dichloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[5-(2-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[2-(4-chloro-phenyl)-thiazol-4-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[5-(4-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[3-(4-chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[3-(4-chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

6-(4-Amino-5-phenyl-4H-[1,2,4]triazol-3-ylsulfanyl)-3-benzyl-5-methyl-1H-pyrimidine-2,4-dione;

or a pharmaceutically acceptable salt thereof.

8. The compound according to Claim 1, selected from:

3-Benzyl-5-methyl-6-[5-(2-methylsulfanyl-pyridin-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-pyrimidine-2,4-dione;

3-Benzyl-5-methyl-6-(3-phenyl-isoxazol-5-ylmethylsulfanyl)-1H-pyrimidine-2,4-dione;

3-Benzyl-5-methyl-6-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-1H-pyrimidine-2,4-dione;

3-Benzyl-5-methyl-6-(5-phenyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-1H-pyrimidine-2,4-dione;

3-Benzyl-5-methyl-6-(2-phenyl-thiazol-4-ylmethylsulfanyl)-1H-pyrimidine-2,4-dione;

3-Benzyl-5-methyl-6-[3-(4-nitro-benzyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[5-(4-chloro-phenylamino)-2H-[1,2,4]triazol-3-ylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

6-(Benzothiazol-2-ylsulfanyl)-3-benzyl-5-methyl-1H-pyrimidine-2,4-dione; and

3-Benzyl-6-(6-methoxy-benzothiazol-2-ylamino)-5-methyl-1H-pyrimidine-2,4-dione;

or a pharmaceutically acceptable salt thereof.

9. The compound according to Claim 1, selected from:

3-Benzyl-6-[3-(2,6-dichloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-1,5-dimethyl-1H-pyrimidine-2,4-dione;

3-Benzyl-1,5-dimethyl-6-[5-(3-methyl-4-nitro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-1H-pyrimidine-2,4-dione;

3-Benzyl-1,5-dimethyl-6-[5-naphthalen-2-yl-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-1H-pyrimidine-2,4-dione;

3-Benzyl-1,5-dimethyl-6-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-1H-pyrimidine-2,4-dione; and

3-Benzyl-1,5-dimethyl-6-[3-(4-nitro-benzyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-1H-pyrimidine-2,4-dione;

or a pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

11. The pharmaceutical composition according to Claim 10, comprising a compound according to any one of Claims 7 to 9, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

12. A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

13. The method according to Claim 12, wherein the compound administered is a compound according to any one of Claims 7 to 9, or a pharmaceutically acceptable salt thereof.